UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/821,719	03/29/2001	Kathleen A. Donovan	07039-260001	4609

26191 7590 05/05/2004

FISH & RICHARDSON P.C.
3300 DAIN RAUSCHER PLAZA
60 SOUTH SIXTH STREET
MINNEAPOLIS, MN 55402

EXAMINER	
HILL, MYRON G	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/821,719	DONOVAN ET AL.	
	Examiner	Art Unit	
	Myron G. Hill	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4, 5, 8, 15, and 30- 44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4, 5, 8, 15, and 30- 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to paper filed 28 December2003, which also added claims 41- 44.

Claims 4, 5, 8, 15, and 30- 44 are under consideration in this action.

Rejections Withdrawn

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 4, 5, 8, 15, and 30- 40 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims have been amended to clarify what is meant by "bone marrow preparation" and the reference to the condition. The steps are clear now.

Claims 4, 5, 8, 15, and 30- 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant has amended the claims to remove "monitor" and add "likely to progress" which is supported in the specification.

Rejections Maintained

Claim Rejections - 35 USC § 103

Claims 4, 5, 8, 15, and 30- 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Donovan *et al.* and Carter *et al.*

The claims are drawn to methods using the steps of assaying for IL-6 in stromal cells for determining if an individual with a MMRPD (multiple myeloma related plasmaproliferative disorder) has a change in IL-6 which measures IL-1beta and indicates a change in disease state or presence of condition when compared to normal.

Applicant argues that there must be some motivation to modify the references and there must be an expectation of success and that the prior art must suggest the desirability of the combination. Applicant asserts that Donovan *et al.* uses a direct assay, does not suggest using normal stromal cells, and does not suggest an assay to evaluate the likelihood of progression to MM. Additionally, Applicant argues that Carter *et al.* fails to correct the deficiencies of Donovan *et al.*

Applicant's arguments have been fully considered and not found persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208

USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Donovan *et al.* do teach that IL-1 beta can differentiate between diagnoses of MM, MGUS, and an unrelated condition (Table 4) and that IL-1 beta and IL-6 have a functional relationship in the cause of and progression to MM (Figure 4 and page 598, column 2- page 599, column 1). Donovan *et al.* disclose and concur that Carter *et al.* teach that the IL-6 production from myeloma cells in stromal culture is specifically the product of the IL-1beta produced by the myeloma cells and that IL-6 was only detected in myeloma cells that were not purified (page 599, column 1, top).

Donovan *et al.* do not teach stromal cell assay.

Carter *et al.* teach a stromal cell assay using purified myeloma cells (MC) and normal marrow stromal cells (MSC), that IL-6 is produced in direct proportion to IL-1 beta in the co-culture, and that the production of IL-6 is blocked by anti-IL1 beta antibodies (page 424- 425, Figure 1, and Table 3, also commented on by Donovan, page 599, column 1, top). Carter *et al.* use commercial stromal cells and not stromal cells from a myeloma patient.

One of ordinary skill in the art at the time of the invention would have known from the teaching of Donovan that evaluating the status of individuals with MGUS (Table 4) or pre-MM conditions such as SMM (Donovan, Table 1) could have their status monitored or compared to controls because the level of IL1 beta goes from undetectable to detectable. One of ordinary skill in the art would know that IL-1 is

secreted so a cell free supernatant of the MC can be assayed for the presence of IL-1 as well. Both references teach purifying the myeloma cells.

One of ordinary skill in the art at the time of invention would be motivated to make this combination because it would allow the assay for IL-1beta to be done without flow cytometry, plasma labeling and hybridization as taught by Donovan *et al.* The assay could be done with commercially available stromal cells and commercially available IL-6 ELISA assays. IL-6 ELISA assays are easy to perform and can be readily automated if required by the facility doing the assays.

Thus, it would have been *prima facie* obvious to use IL-1 beta as taught by Donovan *et al.* with the assay of Carter *et al.* to determine the IL-1 beta level in patients with MMPD with the expectation of success by measuring IL-6 to evaluate if IL-1 beta is in a sample.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 571-272-0901. The examiner can normally be reached on 9am-6pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Myron G. Hill
Patent Examiner
14 April 2004

JAMES HOUSEL 5/3/04
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600